The claims of the published PCT Application are being amended to address issues of a procedural nature and to place the claims in better form for entry into the U.S. national stage.

Should formal amendments to the specification be necessary to conform to U.S. practice, Applicants seek to introduce such amendments into the present specification by, *e.g.*, deleting the PCT cover page, providing the Abstract as a separate page, and deleting the PCT header. The amended abstract included herewith complies with the new rules, as it is 200 words.

Priority is also properly claimed by an amendment at page 1.

II. National Stage Claims

After according a U.S. filing date, and **before** calculating the filing fee, entry of the foregoing claim amendments is respectfully requested.

The published PCT Application includes claims 1-35. Amendments to claims 1, 16 and 30 were made during PCT examination, as reflected in the IPER. However, as the IPER does not show the nature of the amendments with brackets and/or underlining, for the convenience of the U.S. examiner, the unamended claims of the published PCT Application form the initial basis of the present claims. The present amendments to the published PCT claims are clearly shown in the exhibits attached hereto.

The changes to the claims of the published PCT Application are being made to place the claims in better form for entry into the U.S. national stage, *e.g.*, by addressing issues of a procedural nature and correcting minor grammatical errors. The revised claims are fully supported by the specification and claims of the international application and do not in any way constitute new matter.

III. Status of the Claims

In the published PCT Application, claims 1-35 were pending. At the conclusion of the PCT examination phase, as indicated in the enclosed IPER, claims 1, 16 and 30 had been amended. All claims have unity of invention.

Presently, starting from the claims of the published PCT Application, claims 1, 6, 8, 10, 11, 14-30 and 32-34 have been amended to correct minor typographical oversights, to remove multiple dependencies and otherwise place the claims in better form for U.S. practice. No claims have been canceled or added. Claims 1-35 are therefore in the case.

IV. Support for the Claims

Aside from the procedural changes and typographical corrections, current claims 1-35 represent the claims at the conclusion of PCT examination. The changes generally fall into the following categories: to match the clarifications made during the PCT stage (claims 1 and 16), to correct minor typographical oversights (claims 10, 15, 16, 22, 23, 24 and 30), to accord with U.S. statutory subject matter (claim 34) and to remove multiple dependencies for U.S. practice (the remaining amended claims).

Support for the claim revisions largely exists in the amended claims themselves, as supplemented by original claims and specification as filed.

In particular, "composition" has been added to claim 1, and "delivery vehicle" has been changed to "combination product" in claim 16, each of which clarifications reflect those in the PCT phase.

Claims 10, 15 and 16 have been revised to correct minor grammatical errors in connection with "medicament (a) is in micronised form" and "one or more of said antiasthma drugs", respectively.

In claims 22, 23 and 24, the original language "the or each" has been improved by inserting another instance of "individual dose", so that the text now reads "the individual dose or each individual dose".

Claim 30 has been revised to add "composition" after the second instance of SAPL, as in claim 1, and to add "of the SAPL composition" in the last clause, which corresponds to a clarification made in the PCT phase.

Finally, claim 34 has been revised to change the non-statutory second medical use claim format into a composition claim drawn to the recited medicament, in accordance with 35 U.S.C. § 101.

The remaining changes to the revised claims simply remove the multiple dependencies, and such changes are clearly supported by each claim itself.

It will therefore be understood that no new matter is encompassed by any of the amended claims.

V. <u>Compliance with 37 C.F.R. § 1.121</u>

Copies of the pending claims are attached hereto as **Exhibit A** and **Exhibit B**. In accordance with 37 C.F.R. § 1.121, the claims have been labeled as "(Amended)", where appropriate. **Exhibit A** provides a clean copy of the pending claims, whereas **Exhibit B** shows the changes with brackets and underlining in reference to the claims published in the PCT application. As the claims with the IPER were not annotated, this is believed to the best mechanism for complying with 37 C.F.R. § 1.121.

The proper claim for priority has been timely introduced into the specification by amendment of the opening paragraph at page 1. An Abstract of less than 200 words is also introduced into the specification by amendment as a separate page.

The amendments to the opening paragraph at page 1 of the specification and the abstract have been made as "Replacement Sections" in accordance with 37 C.F.R. §§ 1.121(b)(2), 1.77(b)(2) and 1.77(b)(10). This is proper under 37 C.F.R. §§ 1.121(b)(2)(i)(ii)(iii) as the amendments include specific instructions, replacement section in clean form and another version of the replacement section separate from the amendment marked up to show all changes (**Exhibit C**).

VI. Fees and Formalities

The national filing fee and claim fees are included herewith. The fees have been calculated **after** the changes to remove most multiply dependent claims. Any omitted fees should be deducted from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4040.000300.

The claim fees have been calculated according to the following designations: independent, claims 1, 28, 29, 30, 31, 34 and 35; multiply dependent, claims 26, 27 and 33; and dependent, claims 2-25 and 32. Although claims 28 and 29 include a reference to claims 1 or 2 within the body of the claim, these are not multiply dependent claims as the preamble of each claim ("a pack" and "a method") shows that the claims do not depend from the "combination products" of claims 1 and 2. Nonetheless, as established in the PCT phase, all pending claims define a unified invention.

Should the Examiner have any questions or comments, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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Date: May 22, 2001

EXHIBIT A
PENDING CLAIMS

1. (Amended) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug, wherein ingredients (a) and (b) are provided in a form for administration together or separately.

2. A combination product as claimed in claim 1, in which the ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate.

3. A combination product as claimed in claim 2, in which medicament (a) comprises said first component and said second component in a weight ratio of from 1:9 to 9:1.

4. A combination product as claimed in claim 3, in which the proportion by weight of said first component exceeds that of said second component.

5. A combination product as claimed in claim 4, in which said first component and said second component are present in a weight ratio of from 6:4 to 8:2.

6. (Amended) A combination product as claimed in claim 2, in which the medicament (a) comprises a phosphatidyl glycerol.

7. A combination product as claimed in claim 6, in which the phosphatidyl glycerol comprises one or more diacyl phosphatidyl glycerols, of which at least a proportion of the acyl groups are unsaturated.

8. (Amended) A combination product as claimed in claim 2, in which the medicament (a) comprises one or more compounds selected from the group consisting of diacyl phosphatidyl cholines.

9. A combination product as claimed in claim 8, in which the medicament (a) comprises dipalmitoyl phosphatidyl choline.

10. (Amended) A combination product as claimed in claim 2, in which the medicament (a) is in micronised form.

11. (Amended) A combination product as claimed in claim 2, in which said medicament (a) has a median particle size not exceeding 10μm.

12. A combination product as claimed in claim 11, in which said medicament (a) has a median particle size not exceeding 5μm.

13. A combination product as claimed in claim 12, in which said medicament (a) has a median particle size of less than 3 μm.

14. (Amended) A combination product as claimed in claim 2, in which the antiasthma drug comprises one or more respiratory drugs selected from the group consisting of β_2-agonists, steroids, cromones, antimuscarinic drugs and leukotriene receptor antagonists.

15. (Amended) A combination product as claimed in claim 14, which comprises one or more of said antiasthma drugs in an amount of up to 10 parts by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

16. (Amended) A combination product as claimed in claim 15, which comprises one or more of said respiratory drugs in an amount of up to one part by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

17. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a β_2-agonist.

18. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a steroid.

19. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a cromone.

20. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a leukotriene receptor antagonist.

21. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises an antimuscarinic drug.

22. (Amended) A combination product as claimed in claim 2, in which at least ingredient (a) is arranged to be delivered to a patient in the form of at least one individual inhalable dose, the individual dose or each individual dose comprising said ingredient (a) in an amount of at least 10mg.

23. (Amended) A combination product as claimed in claim 22, in which the individual dose or each individual dose comprises said first and second components in a combined amount of at least 25mg.

24. (Amended) A combination product as claimed in claim 23, in which the individual dose or each individual dose comprises said ingredient (a) in a combined amount of at least 40mg.

25. (Amended) A combination product as claimed in claim 22, in which at least ingredient (a) is arranged for sequential delivery of a multiplicity of inhalable doses.

26. (Amended) A combination product as claimed in claim 1 or claim 2, in which the antiasthma drug is arranged for delivery in admixture with ingredient (a).

27. (Amended) A combination product as claimed in claim 1 or claim 2, in which the antiasthma drug is arranged for delivery separately from, and simultaneously or sequentially with, ingredient (a).

28. (Amended) A pack for use as part of a combination product according to claim 1 or claim 2, said pack including a delivery device for delivery of ingredient (a) to a patient and further comprising instructions to use said delivery device in a method of treatment including the separate simultaneous or sequential administration of an antiasthma drug.

29. (Amended) A method of prevention and/or treatment of asthma, comprising administering to a patient at least one dose of a combination product as defined in claim 1 or claim 2.

30. (Amended) A delivery device for administering to a patient by inhalation a medicament for the prevention and/or treatment of asthma, the delivery device containing a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances the spreading of the medicament, the delivery device being arranged for delivery of at least one individual dose of the SAPL composition in an amount of at least 10mg.

31. A delivery device for administering to a patient by inhalation a medicament for the prevention or treatment of asthma, the delivery device containing a medicament comprising a first component consisting of one or more phosphatidyl cholines and a second component consisting of one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate, the delivery device being arranged for delivery of at least one individual inhalable dose, the or each individual dose comprising said first component and said second component in a combined amount of at least 10mg.

32. (Amended) A delivery device as claimed in claim 30, in which the medicament is as defined in claim 2.

33. (Amended) A delivery device as claimed in claim 30 or 31, which further includes means for dispensing an inhalable dose of an antiasthma drug.

34. (Amended) A medicament for use in the control of asthma, comprising (a) a surface active phospholipid (SAPL) composition in finely divided form conjointly with (b) an antiasthma drug.

35. A combination product for use in the prevention or treatment of asthma comprising

(a) a medicament comprising a first phospholipid component which is capable of binding to lung tissue and a second component which is capable of enhancing the spreading of said first component over an aqueous medium at 37°C, said medicament being in the form of a finely divided powder; and

(b) an antiasthma drug;

the ingredients (a) and (b) being arranged for administration in combination or separately, simultaneously or sequentially.

EXHIBIT B
PENDING CLAIMS

1. (Amended) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug, wherein ingredients (a) and (b) are provided in a form for administration together or separately.

2. A combination product as claimed in claim 1, in which the ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate.

3. A combination product as claimed in claim 2, in which medicament (a) comprises said first component and said second component in a weight ratio of from 1:9 to 9:1.

4. A combination product as claimed in claim 3, in which the proportion by weight of said first component exceeds that of said second component.

5. A combination product as claimed in claim 4, in which said first component and said second component are present in a weight ratio of from 6:4 to 8:2.

6. (Amended) A combination product as claimed in [any one of claims 1 to 5] claim 2, in which the medicament (a) comprises a phosphatidyl glycerol.

7. A combination product as claimed in claim 6, in which the phosphatidyl glycerol comprises one or more diacyl phosphatidyl glycerols, of which at least a proportion of the acyl groups are unsaturated.

8. (Amended) A combination product as claimed in [any one of claims 1 to 7] claim 2, in which the medicament (a) comprises one or more compounds selected from the group consisting of diacyl phosphatidyl cholines.

9. A combination product as claimed in claim 8, in which the medicament (a) comprises dipalmitoyl phosphatidyl choline.

10. (Amended) A combination product as claimed in [any one of claims 1 to 9] claim 2, in which the medicament (a) is in micronised form.

11. (Amended) A combination product as claimed in [any one of claims 2 to 10] claim 2, in which said medicament (a) has a median particle size not exceeding 10μm.

12. A combination product as claimed in claim 11, in which said medicament (a) has a median particle size not exceeding 5μm.

13. A combination product as claimed in claim 12, in which said medicament (a) has a median particle size of less than 3 μm.

14. (Amended) A combination product as claimed in [any one of claims 1 to 13] claim 2, in which the antiasthma drug comprises one or more respiratory drugs selected from the group consisting of β_2-agonists, steroids, cromones, antimuscarinic drugs and leukotriene receptor antagonists.

15. (Amended) A combination product as claimed in [any one of claims 1 to 14] claim 14, which comprises one or more of said antiasthma drugs in an amount of up to 10 parts by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

16. (Amended) A [delivery device] combination product as claimed in claim 15, which comprises one or more of said respiratory drugs in an amount of up to one part by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

17. (Amended) A combination product as claimed in [any one of claims 1 to 16] claim 14, in which ingredient (b) comprises a β_2-agonist.

18. (Amended) A combination product as claimed in [any one of claims 1 to 16] claim 14, in which ingredient (b) comprises a steroid.

19. (Amended) A combination product as claimed in [any one of claims 1 to 16] claim 14, in which ingredient (b) comprises a cromone.

20. (Amended) A combination product as claimed in [any one of claims 1 to 16] claim 14, in which ingredient (b) comprises a leukotriene receptor antagonist.

21. (Amended) A combination product as claimed in [any one of claims 1 to 16] claim 14, in which ingredient (b) comprises an antimuscarinic drug.

22. (Amended) A combination product as claimed in [any one of claims 1 to 21] claim 2, in which at least ingredient (a) is arranged to be delivered to a patient in the form of at least one individual inhalable dose, the individual dose or each individual dose comprising said ingredient (a) in an amount of at least 10mg.

23. (Amended) A combination product as claimed in claim 22, in which the individual dose or each individual dose comprises said first and second components in a combined amount of at least 25mg.

24. (Amended) A combination product as claimed in claim 23, in which the individual dose or each individual dose comprises said ingredient (a) in a combined amount of at least 40mg.

25. (Amended) A combination product as claimed in [any one of claims 22 to 24] claim 22, in which at least ingredient (a) is arranged for sequential delivery of a multiplicity of inhalable doses.

26. (Amended) A combination product as claimed in [any one of claims 1 to 25] claim 1 or claim 2, in which the antiasthma drug is arranged for delivery in admixture with ingredient (a).

27. (Amended) A combination product as claimed in [any one of claims 1 to 26] claim 1 or claim 2, in which the antiasthma drug is arranged for delivery separately from, and simultaneously or sequentially with, ingredient (a).

28. (Amended) A pack for use as part of a combination product according to [any one of claims 1 to 27] claim 1 or claim 2, said pack including a delivery device for delivery of ingredient (a) to a patient and further comprising instructions to use said delivery device in a method of treatment including the separate simultaneous or sequential administration of an antiasthma drug.

29. (Amended) A method of prevention and/or treatment of asthma, comprising administering to a patient at least one dose of a combination product as defined in [any one of claims 1 to 27] claim 1 or claim 2.

30. (Amended) A delivery device for administering to a patient by inhalation a medicament for the prevention and/or treatment of asthma, the delivery device containing a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances the spreading of the medicament, the delivery device being arranged for delivery of at least one individual dose of the SAPL composition in an amount of at least 10mg.

31. A delivery device for administering to a patient by inhalation a medicament for the prevention or treatment of asthma, the delivery device containing a medicament comprising a first component consisting of one or more phosphatidyl cholines and a second component consisting of one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate, the delivery device being arranged for delivery of at least one individual inhalable dose, the or each individual dose comprising said first component and said second component in a combined amount of at least 10mg.

32. (Amended) A delivery device as claimed in claim 30 [or claim 31], in which the medicament is as defined in [any one of claims 2 to 18] claim 2.

33. (Amended) A delivery device as claimed in [any one of claims 30 to 32] claim 30 or 31, which further includes means for dispensing an inhalable dose of an antiasthma drug.

34. (Amended) [Use of] A medicament for use in the control of asthma, comprising (a) a surface active phospholipid (SAPL) composition in finely divided form conjointly with (b) an antiasthma drug [in the manufacture of a medicament for the control of asthma].

35. A combination product for use in the prevention or treatment of asthma comprising

(a) a medicament comprising a first phospholipid component which is capable of binding to lung tissue and a second component which is capable of enhancing the spreading of said first component over an aqueous medium at 37°C, said medicament being in the form of a finely divided powder; and

(b) an antiasthma drug;

the ingredients (a) and (b) being arranged for administration in combination or separately, simultaneously or sequentially.

EXHIBIT C
REPLACEMENT SECTIONS

In the Section of the Application pertaining to "Cross-reference to Related Applications", the deletions and additions are as shown:

The present application is a nationalization of International Patent Application PCT/GB99/03952, filed November 26, 1999, which claims priority to British Patent Application 9912639.3, filed May 28, 1999 and to International Patent Application PCT/GB98/03543, filed November 26, 1998.

Field of the Invention

This invention relates to pharmaceutical products for use in the treatment of asthma and to delivery devices including the products.

In the Section of the Application pertaining to "Cross-reference to Related Applications", the final text is as follows:

The present application is a nationalization of International Patent Application PCT/GB99/03952, filed November 26, 1999, which claims priority to British Patent Application 9912639.3, filed May 28, 1999 and to International Patent Application PCT/GB98/03543, filed November 26, 1998.

Field of the Invention

This invention relates to pharmaceutical products for use in the treatment of asthma and to delivery devices including the products.

ABSTRACT

In the Section of the Application that forms the Abstract, the deletions and additions are as shown:

ABSTRACT

[A] Disclosed is a combination product for use in treating asthma and other respiratory conditions comprising a medicament comprising a surface active phospholipid composition in the form of a fine powder and an antiasthma drug. The product is arranged to be administered to the lungs by inhalation, for example, by [a device 1] the disclosed devices.